IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re:	**US 5,674,860**
Issued:	**October 7, 1997**
To:	**Christer Carl Gustav Carling; Jan William Trofast**
For:	**Combination of a Bronchodilator and a Steroidal Anti-Inflammatory Drug for the Treatment of Respiratory Disorders**

CERTIFICATE OF EFS-WEB TRANSMISSION

I hereby certify that this paper is being transmitted via the Electronic Filing System to the U.S. Patent and Trademark Office on the date indicated below.

/John M. Genova/	32,224
Signature	Reg. No.
John M. Genova	December 16, 2008
Signer's Name	Date

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Commissioner for Patents
Box 1450
Alexandria, VA 22313-1450

REQUEST FOR RECONSIDERATION OF FINAL DETERMINATION

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OF FINAL DETERMINATION

Sir:

On June 13, 2008, the United States Patent and Trademark Office ("PTO") issued a Notice of Final Determination (the "Notice") alleging that US 5,674,860 (the "'860 patent") is not eligible for patent term extension ("PTE") under 35 U.S.C. § 156 based upon the approval of a fixed-dose combination product Symbicort®. Symbicort was approved under Section 505(b) of the Federal Food, Drug and Cosmetic Act and received permission for commercial marketing or use by the Food and Drug Administration ("FDA") in a letter dated July 21, 2006. The PTE application was filed September 19, 2006.

The determination of ineligibility for patent term is based upon the PTO's position that Symbicort does not constitute the first permitted commercial marketing or use of the approved product Symbicort (formoterol fumarate dihydrate and budesonide) and that the PTE application was not timely filed.

A. Synergistic Combination

Symbicort is the first approved product that is a fixed-dose combination of budesonide and formoterol fumarate dihydrate. This combination has an unexpected synergistic effect when compared to the monoproducts and an unexpectedly beneficial pharmacological interaction, as demonstrated by the clinical evidence provided in the PTE application. The PTO does not dispute the synergistic effect of Symbicort. Rather, in denying the PTE application, the PTO relies on *In re Alcon Labs. Inc.*, 13 USPQ2d 1115, 1118 (Comm'r Pat. & Trademarks 1989), and *Arnold Partnership* v. *Dudas*, 362 F.3d 1338, 1343 (Fed. Cir. 2004), for restricting the determination of PTE eligibility to a component-by-component verification of prior FDA approval. However, neither *Alcon Labs* nor *Arnold Partnership* is conclusive on the eligibility of combination drug patents such as the '860 patent for PTE under 35 U.S.C. §156.

Specifically, in *Alcon Labs*, the Commissioner's negative decision was based - not on synergy - but on a faulty interpretation of the legislative history of 35 U.S.C. §156(a)(5)(A) together with 35 U.S.C. §156(f)(2), resulting in his conclusion that "patent term extension should be available only to active ingredients that are [new chemical entities ("NCEs")] - approved by the FDA for the *first* time." *In re Alcon Labs. Inc.*, 13 USPQ 2d at 1120 (emphasis in original). This interpretation – which the PTO relies upon in the Notice – is inconsistent with *Glaxo Operations UK Ltd.* v. *Quigg*, 894 F.2d 392, 397 (Fed. Cir. 1990), which rejected the Commissioner's interpretation of Congress' intent that "product," as defined by 35 U.S.C. §156(f)(1)-(2), is limited to NCEs for purposes of PTE eligibility.

Similarly, in *Arnold Partnership*, synergy and a combination drug patent's eligibility for PTE were never squarely addressed on the merits. The Court acknowledged that the PTO had not taken a position regarding synergy in denying PTE. *Arnold Partnership*, 362 F.3d at 1342. In affirming the denial, the Court looked beyond the PTE application to certain statements from the specification of the patent at issue of an alleged interaction between the constituents but without any mention of synergy. *Id.* In *dicta*, the Court stated that "this court doubts that synergistic

effects are an appropriate distinction for term extension policies. . . ." *Arnold Partnership*, 362 F.3d at 1343. In so doing, the Court did not reject the eligibility of a drug combination patent for PTE eligibility. This is consistent with Section 2751 of the Manual of Patent Examining Procedure ("MPEP"), which does not expressly negate the eligibility for PTE under 35 U.S.C. §156 of an approved product having two active ingredients that are shown to have a synergistic effect or have a beneficial pharmacological interaction.

In conclusion, none of the support cited by the PTO in the Notice is analogous to the facts at hand. Specifically, the Symbicort PTE application provides conclusive evidence demonstrating that administration of a fixed-dose combination of budesonide and formoterol leads to an unexpected synergistic effect such that the resultant pharmacologic effects are greater than the sum of their constituents. In view of that proof and the opportunity left open by *Arnold Partnership,* it is submitted that Symbicort - consistent with MPEP §2751 - is the drug product that should be considered to have a single new active ingredient that has not been previously approved for commercial marketing and use.

B. Timeliness

The FDA approval letter for Symbicort was dated July 21, 2006. The Symbicort PTE application was filed with the PTO on September 19, 2006, i.e., within 60 days of FDA approval. When it filed the Symbicort PTE application in September 2006, the Applicant - AstraZeneca AB - followed the same method of determining the filing period that it had previously used in 1991 and in 2003, as follows:

- in 1991 when it filed a PTE application that was granted in 1993 for US 4,215,113, in connection with its approved Foscavir® drug product; the PTE application was filed on November 26, 1991, within 60 days of FDA approval on September 27, 1991; and

- in 2003, when it filed a PTE application that the PTO and the FDA both indicated in letters in 2004 to have been timely filed; the PTE application was filed on August 19, 2003, in connection with Prilosec® OTC, within 60 days of FDA approval on June 20, 2003. Two years *after* the filing of the Symbicort PTE application, both agencies inexplicably reversed their previous position and informed Applicant that its Prilosec OTC PTE application was not timely filed. This issue of timeliness with respect to the Prilosec OTC PTE application is the subject of a pending Petition to the Director, submitted to the PTO on May 30, 2008, and incorporated herein by reference.

In addition, there is legal precedent, *Alcon Labs*, for determining the filing period as AstraZeneca has for the Symbicort PTE application. The PTE application that was the subject of the 1989 *Alcon Labs* decision, discussed *supra,* was filed the same number of days after FDA approval as was the Symbicort PTE application. FDA approval of Tobradex, the subject drug in *Alcon Labs,* was granted on August 18, 1998; the subject PTE application was filed with the PTO on October 17, 1998. Commissioner Quigg found the Tobradex PTE application, which was filed within 60 days of FDA approval, ***"excluding"*** the day of FDA of approval, "to comply with the requirements of 37 C.F.R. §156(d) and the provisions of 37 C.F.R. §§1.740 and 1.741. *Alcon Labs. Inc.*, 13 USPQ2d at 1116.

Moreover, at no time prior to the filing of its Symbicort PTE application in 2006 did the PTO inform Applicant, Applicants' registered patent attorneys or the general public that it had changed its method of determining timeliness such as set forth in 1987, in the *Memorandum of Understanding Between The Patent and Trademark Office and The Food and Drug Administration* (the "*1987 Memorandum of Understanding*"), MOU 225-86-8251, 52 Fed. Reg. 17830 (May 12, 1987), which instructs the FDA to inform the PTO whether a PTE application is timely filed within 60 days ***after*** the product was approved. The FDA's "Frequently Asked Questions on the Patent Term Restoration Program" echoes the same method as the *1987 Memorandum of Understanding.*

Despite clear evidence to the contrary, including the legal precedent of *Alcon Labs*, the PTO maintains that the governing authority for timely filing, i.e., section 156(d)(1) and Rule 1.720(f), by its plain language, is clear. However, the PTO itself has, since 1986 until October 2007, granted PTE to applicants who filed within 60 days of FDA approval, counting day 1 (of the 60 days) as the day after FDA approval, as demonstrated by the following twelve (12) third-party patents: US 3,721,687; US 3,732,340; US 4,407,288; US 4,513,006; US 4,702,253; US 4,830,010; US 4,836,217; US 4,941,093; US 5,441,745; US 5,532,221; US 5,639,639; and US 5,827,937.

In sum, when it filed its Symbicort PTE application, Applicant relied on its own 18+ years of experience with the PTO's long-standing practices and believed that its PTE application was timely filed. There is no basis today for the PTO to change, without proper notice, its method of determining timeliness, and it is respectfully requested that the Symbicort PTE application be found to have been timely filed in view of the reasons set forth herein and in the Petition.

C. Petition for Extension of Time

AstraZeneca herewith petitions the Commissioner for Patents to extend the time for this Request in response to the Notice of Final Determination, mailed June 13, 2008, for five (5) months from August 13, 2008, to January 13, 2009. Authorization is given to charge the corresponding extension of time fee pursuant to 37 C.F.R. § 1.136(a), and any other required fee in connection with this communication, to Deposit Account No. 23-1703. Any deficiency or overpayment should be charged or credited to the above numbered deposit account.

Respectfully submitted,

Dated: December 15, 2008

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